## REMARKS

Claims 2-7 and 9 are pending in the instant application. Applicants believe that the arguments and remarks made herein place all pending claims in condition for allowance.

### 1. THE REJECTIONS UNDER 35 U.S.C. §112, FIRST PARAGRAPH, FOR LACK OF ENABLEMENT SHOULD BE WITHDRAWN

Claims 2-7 and 9 are rejected under 35 U.S.C. §112, first paragraph, because the specification allegedly does not enable any person skilled in the art to which it pertains or with which it is most nearly connected to make the invention commensurate in scope with the claims. As discussed in detail below, the applicants disagree with the Examiner's contentions and submit that the claims are enabled and should be allowed.

### A. The Legal Standard

The test for enablement is whether one reasonably skilled in the pertinent art could make or use the invention, without undue experimentation, from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. *U.S. v. Telectronics Inc.*, 857 F.2d 778, 8 USPQ2d 1217 (Fed. Cir. 1988). In fact, well-known subject matter is preferably omitted. See *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986) ("a patent need not teach, and preferably omits, what is well known in the art."). See *Northern Telecom, Inc. v. Datapoint Corp.*, 908 F.2d 931, 941 (Fed. Cir. 1990). These enablement rules preclude the need for the patent applicant to "set forth every minute detail regarding the invention." *Phillips Petroleum Co. v. United States Steel Corp.*, 673 F. Supp. 1278,

1291 (D. Del. 1991); see also *DeGeorge v. Bernier*, 768 F.2d 1318, 1323 (Fed. Cir. 1985).

Undue experimentation is experimentation that would require a level of ingenuity beyond what is expected from one of ordinary skill in the field. *Fields v. Conover*, 170 USPQ 276, 279 (CCPA 1971). The factors that can be considered in determining whether an amount of experimentation is undue have been listed in *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Among these factors are: the amount of effort involved, the guidance provided by the specification, the presence of working examples, the amount of pertinent literature and the level of skill in the art. The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, so long as it is merely routine. *Id.*

Further, while the predictability of the art can be considered in determining whether an amount of experimentation is undue, mere unpredictability of the result of an experiment is not a consideration. Indeed, the Court of Custom and Patent Appeals specifically cautioned that the unpredictability of the result of an experiment is not a basis to conclude that the amount of experimentation is undue:

> [If to fulfill the requirements of 112, first paragraph, an applicant's] disclosure must provide guidance which will enable one skilled in the art to determine, with reasonable certainty before performing the reaction whether the claimed product will be obtained, ... then all "experimentation" is "undue" since the term "experimentation" implies that the success of the particular activity is uncertain. Such a proposition is contrary to the basic policy of the Patent Act.
> *In re Angstadt*, 190 USPQ 214 (CCPA 1976), at 219.

Thus, all that is required is a reasonable amount of guidance with respect to the direction of the experimentation; reasonable certainty with regard to the outcome of the experimentation is not required.

In addition, the Patent and Trademark Office bears the initial burden of establishing a *prima facie* case of non-enablement. *In re Marzocchi*, 169 USPQ 367, 369 (C.C.P.A. 1971); M.P.E.P. § 2164.02. A patent applicant's specification which contains a teaching of how to make and use the invention must be taken as enabling unless there is reason to doubt the objective truth of the teachings which must be relied on for enabling support. *Id.*

**B. The Prosecution History**

At the outset, applicants believe a brief review the history of the current rejections will be beneficial to both the Examiner and applicant in advancing prosecution of the application.

*Claims 2, 3, 5-7, and 9* In the Office Action dated November 1, 2002 and the Office Action dated July 15, 2003, claims 2 and 3 were rejected for lack of enablement based on the Examiner's contention that specification was not commensurate in scope with the claims with respect to the term "damaged or injured central nervous system tissue." In particular, the Examiner indicated that the specification was enabling for "a method for enhancing the function of normal excitable tissue in a mammal," but that it was not enabling for "a method for enhancing the function of *abnormal excitable tissue* in a mammal". (*See* pages 5-6, of the Office Action dated November 1, 2002, and page 3, lines 1-7, of the Office Action dated July 15, 2003) (emphasis in original). Likewise, with respect to claims 5-7 and 9, the Examiner indicated that the specification was enabling for "a method for enhancing the function of normal excitable tissue in a mammal" but that it was not enabling for "a method for enhancing the function of *abnormal excitable tissue* in a mammal". (*See* pages 5-6, of the Office Action dated November 1, 2002, and page 3, lines 1-7, of the Office Action dated July 15, 2003)

(emphasis in original). Thus, the Examiner distinguished between *normal* and *abnormal* excitable tissue with respect to claims 2, 3, 5-7 and 9.

In the Amendment dated January 14, 2004, applicant submitted copending U.S. Patent Application No. 10/188,905, inviting the Examiner to consider Example 9. In response, the Examiner indicated in an Advisory Action dated April 5, 2004 ("the Advisory Action") that Example 9 only correlated to *abnormal tissue* due to *injury*. (*See* page 2, lines 36-37 of the Advisory Action).

In the Amendment dated August 16, 2004, applicants amended claims 2, 3, 5-7 and 9 to replace "abnormal" with "damaged." The Examiner, however, rejected the amended method claims for lack of enablement, stating that the specification was enabling for "a method for enhancing the function of normal or **injured"** tissue in a mammal" but that it was not enabling for "a method for treating the function of normal or **damaged"** tissue in a mammal. (*See* page 3, lines 1-11, of the Office Action dated October 26, 2004 (emphasis in original). The Examiner asserted that "damaged excitable tissue is the end result of many diseases and would still encompass conditions such as stroke, Alzheimer's disease, multiple sclerosis, etc." (*See* page 4, lines 9-11, of the Office Action mailed October 26, 2004).

In the Amendment dated January 25, 2005, applicants continued to pursue claims directed toward "damaged" tissue, directing the Examiner's attention to several post-filing date studies, *i.e.,* Ehrenreich *et al.* 2002, Molec. Med. 8:495-505 ("Ehrenreich") (human stroke patients); Bianchi *et al.*, 2004 Proc. Natl. Acad. Sci USA. 101:823 ("Bianchi") (streptozotocin-induced diabetes in rats); and Agnello *et al.*, 2002, Brain Res. 952:128-134 ("Agnello") (myelin basic protein induced autoimmune encephalomyelitis in rats) to demonstrate the efficacy of the claimed methods in animal

models, and in human subjects, for a number of different conditions involving tissue damaged as a result of various diseases.

The Examiner found the references partly persuasive for claims 2, 3, 5-7, and 9, stating that the while the specification is enabling for "a method of enhancing the function of **normal, damaged or injured excitable tissue** in a mammal, **wherein the damage or injury is caused by stroke, diabetic neuropathy or autoimmune encephalomyelitis**" but that it is not enabling for "a method of enhancing the function of **damaged or injured excitable tissue** in a mammal" (*See* page 3, line1 to page line 4, of Office Action dated April 5, 2005) (emphasis in original).

In the Amendment dated October 5, 2005, applicants submitted additional references, *i.e.,* Lu *et al*, 2005, Journal of Neurotrama 22(9):1011-1017 ("Lu") (traumatic brain injury); Mogensen *et al.*, 2004, Pharmacology, Biochemistry and Behavior 77:381-390 ("Mogensen") (hippocampal lesions); Kumral *et al.*, 2004, Behavioral Brain Res. 153:77-86 ("Kumral") (hypoxia-ischemia); Ehrenreich et al., Molecular Psychiatry (2003), 1-13 ("Ehrenreich") (schizophrenia); van der Meer *et al.*, 2005, JACC 46(1): 125-33 ("van der Meer") (myocardial infarction); and Keswani *et al.*, 2004, Ann. Neurol 56:815-826 ("Keswani") (axonal degeneration) to demonstrate the efficacy of the claimed methods in animal models, and in human subjects, for a number of different conditions involving tissue damage as a result of various diseases. (*See* Office Action dated October 5, 2005).

The Examiner in the next Office Action found, with respect to claims 2 and 3, that the specification was enabling for "a method of enhancing the function of normal, damaged or injured central nervous system tissue in a mammal, **wherein the damage or injury is caused by blunt trauma, stroke or cerebral hypoxia-ischemia**" and with respect to claims 5-7 and 9, that the specification was enabling for "a method of

enhancing the function of normal, damaged or injured excitable tissue in a mammal **wherein the damage or injury is caused by diabetic neuropathy or myocardial infarction,**" but that the specification was not commensurate in scope with the recited claims, *i.e.,* damaged or injured excitable tissue caused by any condition or disease. (*See* page 3, lines 10-18 and page 4, lines 3-9 of the Office Action dated January 9, 2006) (emphasis in original).

In the Amendment dated July 10, 2006, the applicant re-submitted additional post-filing date studies of Lu; Mogensen; Kumral; and Ehrenreich to demonstrate the efficacy of the claimed invention.

In the most recent Office Action, the Examiner stated at page 3, lines 2-3 that claims 2 and 3 are enabling for a limited scope, *i.e.*, "wherein said damage or injury is caused by ***trauma, stroke or cerebral hypoxia-ischemia***" but that claims 2 and 3 are not enabled for the full scope of a method of enhancing the function of normal, damaged, or injured central nervous system tissue (*i.e.*, ***any type of damage or injury*** to the central nervous system) (*See* Office Action dated October 10, 2006, page 5, lines 14-17) (emphasis in original). With respect to claims 5-7 and 9, the Examiner asserts that these claims are enabled for a limited scope, *i.e.,* wherein the "damage or injury is caused by ***sensory axonal degeneration, autoimmune encephalomyelitis, or myocardial infarction***" but not for the full scope of a method of enhancing the function of normal, damaged, or injured excitable tissue in mammal. The Examiner contends that the applicants lack enablement for the genus of damaged or injured excitable tissue caused by any condition or disease.

In summary, the Examiner originally submitted that the claims were enabled for normal excitable tissue but not for abnormal excitable tissue because the specification was not commensurate in scope with claims. Subsequently, the Examiner found the

claims were enabled for normal or injured excitable tissue but not enabled for damaged excitable tissue. The Examiner then found the claims were enabled for normal or injured or damaged excitable tissue but only wherein the damage or injury is caused by stroke, diabetic neuropathy or autoimmune encephalomyelitis. Finally, the Examiner found that the specification enabled the claims wherein the damage or injury is caused by not only stroke but also by blunt trauma, cerebral hypoxia-ischemia, sensory axonal degeneration, autoimmune encephalomyelitis and myocardial infarction.

*Claim 4* With respect to claim 4, the Examiner states that claim 4 is enabling for a limited scope, *i.e.,* "wherein said excitable tissue is central nervous system tissue or ***sensory axonal tissue***" but is not enabled for the full scope of the claim, *i.e.,* any type of damaged/injured peripheral nervous system tissue. (*See* page 6, line 1, to page 7, line 2, of the Office Action dated October 10, 2003). A brief history of this rejection is recited below.

In the Office Action dated April 5, 2005, the Examiner found that claim 4 was enabled for "a method of enhancing the function of **normal, damaged or injured excitable tissue in a mammal, wherein the damage or injury is caused by**..., wherein said excitable tissue is central nervous system tissue or peripheral nervous system tissue" but not enabling for the genus of "**normal, damaged or injured excitable tissue in a mammal.**" (*See* page 3, lines 7-17, and page 4, lines 1-4) (emphasis in original).

In the Amendment dated October 5, 2005, applicants submitted additional references, *i.e.,* Lu, Mogensen, Kumral, Ehrenreich, van der Meer and Keswani, all cited above, to demonstrate the efficacy of the claimed methods in animal models, and in human subjects, for a number of different conditions involving tissue damage as a result of various diseases.

In the Office Action dated January 9, 2006, the Examiner found that claim 4 was enabled for "a method of enhancing the function of normal, damaged, or injured excitable tissue in a mammal,...wherein said excitable tissue is central nervous tissue" but that the specification was not enabling for wherein said excitable tissue is peripheral nervous system tissue.

In the Amendment dated July 10, 2006, applicants submitted additional post-filing date studies including Keswani, full citation provided above, to demonstrate the efficacy of the claimed invention. Keswani teaches that systemic EPO enhances the function of peripheral nervous system tissue, sensory axons and Schwann cells, subjected to peripheral neuropathies and other neurodegenerative diseases. The Examiner found this argument partly persuasive, but, as noted above, has limited the scope of enablement to only sensory axonal tissue.

In summary, applicants initially point out that the Examiner in the Office Action dated April 5, 2005, found that the specification was enabling for "a method of enhancing the function of normal, or damaged, or injured excitable tissue...wherein said excitable tissue is central nervous system tissue or *peripheral nervous system tissue*" (*See* page 3, lines 7-13) (emphasis added), but then in the subsequent Office Action dated January 9, 2006, indicated that claim 4 was only enabled for excitable tissue wherein said excitable tissue is central nervous system tissue. (*See* page 3, 20 – page 4, line 2). As discussed hereafter, applicants respectfully disagree with the Examiner's limited scope of enablement.[1]

[1] Applicants note that although claim 4 contains the language "damaged or injured excitable tissue" as found within claims 5-7 and 9, the Examiner has not rejected claim 4 in the current Office Action for lack of enablement with regards to the causes of such damaged or injured excitable tissue. In the event the Examiner intended to issue such a rejection, Applicants submit the same arguments advanced for claims 5-7 and 9.

## C. Claims 2-7 and 9 Comply With The Enablement Requirement

Claims 2-7 and 9 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Examiner contends that the specification lacks enablement for a genus of "unlimited number" of conditions and diseases with damaged/injured excitable tissue and poor associative learning/memory.

*Claims 2 and 3* In particular, according to the Examiner, claims 2 and 3 are enabling for a limited scope, *i.e.*, "wherein said damage or injury is caused by ***trauma, stroke or cerebral hypoxia-ischemia***" but are not enabled for the full scope of a method of enhancing the function of normal, damaged, or injured central nervous system tissue (*i.e.*, ***any type of damage or injury*** to the central nervous system). (*See* (at page 3, lines 2-3, of the Office Action; page 5, lines 14-17, of Office Action dated October 10, 2006) (emphasis in original). The Examiner has indicated that "[a] disclosure of one example of damaged/injured excitable tissue (stroke) and enhanced function of damaged/injured excitable tissue, associative learning, memory or cognitive function in mammals...is not representative of a genus encompassing an unlimited number of conditions/diseases with damage/injured excitable tissue and poor associative learning/memory." (*See* page 5, lines 8-13, of Office Action dated April 5, 2005). In subsequent Office Actions, in response to the applicants' submission of post-filing date studies, the Examiner found the specification enabling for not only one example (stroke) but also two more examples (blunt trauma and cerebral hypoxia-ischemia). Nonetheless, the Examiner has maintained that the full scope of the claims is not enabled. Applicants respectfully disagree, for the reasons discussed below.

*Claim 4* With regards to claim 4, the Examiner contends that the specification is enabling for sensory axonal tissues, but not any peripheral nervous system tissue.

*Claims 5-7 and 9* According to the Examiner, claims 5-7 and 9 are enabled for a limited scope, *i.e.*, "wherein said damage or injury is caused by ***sensory axonal degeneration, autoimmune encephalomyelitis, or myocardial infarction,***" but are not enabled for the full scope of a method of enhancing the function of normal, damaged, or injured excitable tissue in mammal. Initially, the Examiner indicated "a disclosure of two examples of damaged/injured excitable tissue (diabetic neuropathy and autoimmune encephalomyelitis)[2] and enhanced function of damaged/injured excitable tissue upon EPO is not representative of a genus encompassing an unlimited number of conditions/diseases with damage or injured excitable tissue." (*See* page 5, lines 13-17, of Office Action dated April 5, 2005). In subsequent office actions, in response to the applicants' submission of post-filing date studies, the Examiner found the specification enabling also for sensory axonal degeneration and myocardial infarction.[3] Nonetheless, the Examiner has maintained that the full scope of the claims is not enabled.

First, it is important to note that the methods of claims 2-7 and 9 for the use of peripherally administered EPO are effective for enhancing the function of damaged or injured tissue function *regardless of the cause of the damage or injury to the tissue*. In other words, regardless of how the damage or injury occurred, peripherally administered EPO will work in the same way to enhance the function of the damaged or injured tissue in the mammal. For example, the specification states that "such a molecule may signal via the EPO receptor, for example, initiates a signal transduction cascade ultimately activating a gene expression program resulting in the protection or enhancement of excitable tissue function." *See* page 8, lines 25-28; page 11, line 31 - page 12, line 1.

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[2] As discussed below in *footnote* 3, there were actually three examples.

[3] Although the Examiner in previous Office Actions found the specification enabling for stroke and diabetic neuropathy with respect to the claims 5-7 and 9, the Examiner has currently stated the claims are enabling for sensory axonal degeneration, autoimmune encephalomyelitis, and myocardial infarction.

Moreover, *even if* the mechanism by which the disease or condition causes damaged or injured central nervous system tissue were relevant for determining the enablement of these claims, which is denied, such diseases or conditions use a common pathway that result in the damaged or injured tissue. For example, applicants disclose this common general mechanism at page 1, line 33 – page 2, line 6 of the specification:

> It is widely understood that decreases in energy supplies available to the brain, such as glucose or oxygen, results in profound impairment of brain function, including cognition. Many (but not all) neurons in the central nervous system are easily damaged while working under metabolically-limited conditions, *e.g.*, hypoxia, hypoglycemia, stress and/or prolonged, strong excitation. Under these circumstances, the electrochemical gradients of these cells often collapse, resulting in irreversible neuronal injury and cell death. Current opinion favors this general mechanism as a common final pathway for a wide range of common and debilitating neurological diseases including stroke, epilepsy, and Alzheimer's disease.

Accordingly, one of ordinary skill in the art would expect that if stroke or hypoxia caused damage or injury to central nervous system tissue that could be enhanced by the administration of EPO according to the claimed invention, then other causes that use the same or similar pathway that result in damage or injured tissue would also result in such tissue that could be enhanced according to the claimed invention.

In this regard, Applicants direct the Examiner's attention to a statement made in the Office Action dated October 26, 2004, where it was stated "damaged excitable tissue is the end result of many diseases and would still encompass conditions such as stroke, Alzheimer's disease, multiple sclerosis, etc." (*See* page 4, lines 9-11). Applicants submit that if damaged excitable tissue is the end result, then *how* the central nervous system tissue becomes damaged or injured is not relevant (*e.g.*, stroke, trauma, Alzheimer's disease, multiple sclerosis, schizophrenia) so long as the claimed methods

for peripheral administration of EPO is effective to enhance the damaged or injured tissue.

Second, the applicants submit that the specification of the instant application provides extensive guidance on how to make and use the full scope of the claimed invention. For example, applicants point out that the methods of claims 2 and 3 are methods for enhancing the function of normal, damaged, or injured central nervous system tissue in a mammal "**so that the associative learning or memory in/of the mammal is enhanced**" (as in claim 2) or "**so that the cognitive function is enhanced**" (as in claim 3), respectively (emphasis added). Thus, the claims are directed toward enhancing associative learning or memory in/of the mammal and cognitive function. The specification provides extensive teaching on how to test for enhancement of associative learning or memory and cognitive function in the damaged tissue. For example, the specification describes in detail and provides working examples of use of the Morris Water Maze Test (Example 1, pages 28 - 29) and Conditioned Taste Aversion Test (Example 2, pages 29-31). The specification also states that any other art-accepted learning or cognitive model would be useful in carrying out the claimed methods. (*See* page 11, lines 3-14; page 12, line 25 - page 13, line 11; Examples 1-2).

With regard to claim 4, applicants submit that the specification, together with the Keswani reference would allow one of ordinary skill in the art to make and use the full scope of claim 4 without resort to undue experimentation.

Regarding claims 5-7 and 9, applicants further point out that the specification is enabling for numerous examples of injured and damaged tissue. These include stroke, diabetic neuropathy, sensory axonal degeneration, autoimmune encephalomyelitis, and myocardial infarction. *See footnote 3*. Also, because claims 5-7 and 9 are not limited by the language cited in claims 2 and 3, these claims are also enabled for blunt trauma and

cerebral hypoxia-ischemia. All totaled, there are at least seven different examples of types of conditions that cause damaged or injured excitable tissue. Nonetheless, the Examiner contends, just as for the genus of damaged or injured central nervous system tissue with regards to claims 2 and 3, that applicant has not provided enough examples to be considered representative of the genus of conditions causing damaged or injured excitable tissue.

Thus, although applicants assert that they are not required to disclose every species encompassed by their claims, *see Vaeck*, 947 F.2d at 496, and, that the number of examples they have enabled, *i.e.*, at least seven, in combination with the disclosure of the specification, specifically the testing for enhanced cognitive function and Examples 1 and 2, the applicants submit the specification enables one of ordinary skill in the art to make and use the full scope of the claimed invention without having to engage in undue experimentation.

Moreover, the applicants have provided numerous examples that demonstrate that the claimed methods may be successfully applied, without undue experimentation, regardless of the cause of the tissue injury or tissue damage. To this end, applicants have provided at least three examples of types of conditions that cause damaged or injured central nervous system tissue, *i.e.*, stroke, blunt trauma and cerebral hypoxia-ischemia. Nonetheless, the Examiner essentially contends that this number of examples does not represent the genus of conditions causing damaged or injured central nervous system tissue.

The case law is well-settled that not every species encompassed by the claims needs to be exemplified in the specification, as long as the disclosure teaches how to make and how to use the invention as broadly as it is claimed:

> [T]here must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to

> make and how to use the invention as broadly as it is claimed. This means that the disclosure must adequately guide the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility.
> *In re Vaeck*, 947 F.2d 488, 496 ( Fed. Cir. 1991) (citing *In re Angstadt*, 537 F.2d 498, 502-03 (CCPA 1976).

As discussed above, the specification provides detailed disclosure regarding how to determine which conditions causing damage tissue are encompassed by the claimed genus. Additionally, the specification provides working examples, *i.e.*, Examples 1 and 2. Thus, applicants submit the specification enables one of ordinary skill in the art to make and use the full scope of the claimed invention without having to engage in undue experimentation.

Finally, it is important to note that the Examiner has provided no reason to doubt that the teachings relied on for enabling support will not work across the full scope of the claims. In particular, the Examiner has not cited any reason that to expect that the cause of the excitable tissue damage would alter the effectiveness of EPO in enhancing the function of the damaged or injured tissue. According to applicable case law, the Patent and Trademark Office bears the initial burden of establishing a *prima facie* case of non-enablement. *In re Marzocchi*, 169 USPQ 367, 369 (C.C.P.A. 1971); M.P.E.P. § 2164.02. A patent applicant's specification which contains a teaching of how to make and use the invention must be taken as enabling unless there is reason to doubt the objective truth of the teachings which must be relied on for enabling support. *Id.* In this case, the Examiner has provided no such reason for doubt.

Nevertheless, even if some types of damaged or injured excitable tissue could not be enhanced using the claimed methods, such inoperative embodiments would not render the claim unpatentable for lack of enablement. *See Atlas Powder Co. v. E.I. DuPont,* 750 F.2d 1569, 1576 (Fed. Cir. 1984) (quoting *In re Dinh-Nguyen*, 492 F.2d 856, 858-

859 (CCPA 1974) ( "It is not a function of the claims to specifically exclude...possible inoperative [embodiments].)

Finally, an additional grounds of rejection under 35 U.S.C. § 112, first paragraph applies to claim 5. In particular, the Examiner contends that the specification enables the method of claim 5 only for intravenous and intracranial routes of administration whereby EPO crosses the blood/brain barrier. The Examiner submits that the specification lacks enablement for a method in which EPO crosses the blood/brain barrier via other routes of administration such as oral, topical, intraluminal, inhalation, and parenteral. As discussed hereafter, applicants respectfully disagree.

The specification provides several examples whereby EPO was administered intraperitoneally and was found to enhance the function of normal, damaged, or injured excitable tissue by crossing the blood brain barrier. One of ordinary skill in the art would understand from reading the specification that the intraperitoneally injected EPO entered the blood of the mammal which acted as a conduit to transport the EPO to the brain where it then crossed the blood/brain barrier. Likewise, one of ordinary skill in the art would understand from reading the specification that EPO administered by different routes of administration would also enter the blood and be transported to the brain where it can then cross the blood/brain barrier and that one of ordinary skill in the art could have made and used the claimed invention without undue experimentation by administering EPO using different routes which were known specifically for EPO and generally for other proteins at the time of filing the instant application.[4]

For each of the reasons set forth above, applicants submit that the specification fully describes and enables the methods of claims 5 of the invention and, as such,

[4] In this regard, the Examiner's attention is invited to the 2000 edition of the Physician's Desk References ("PDR"), the art-accepted standard reference manual for practitioners at the relevant time; and, in particular, the section of the PDR relating to erythropoietin (see PDR, pp. 519-525, a copy of which is provided herewith as Exhibit A). The PDR shows that EPO may be administered intravenously or subcutaneously.

respectfully request that the rejection under 35 U.S.C. § 112, first paragraph, lack of enablement, be withdrawn.

Therefore, in summary, applicants submit that, based on the teaching of the specification and the knowledge of skilled artisan, one of ordinary skill in the art would know how to practice the invention within this claim scope. The skilled person could readily determine whether central nervous system excitable tissue is damaged or injured – regardless of the cause of the damage – and, using the known assays disclosed in the specification, he or she would be able to peripherally administer a non-toxic effective amount of recombinant EPO to said mammal. The skilled artisan could then simply determine the enhancement of function of the damaged or injured central nervous system tissue using the methods provided in the specification and known in the art, without resorting to undue experimentation. Based on the results, the skilled artisan would know how to determine which damaged or injured central nervous system tissue that could be enhanced using these methods and could practice the claimed methods within the scope of the claims.

## 2. THE PROVISIONAL OBVIOUSNESS-TYPE DOUBLE-PATENTING REJECTION SHOULD BE WITHDRAWN

Claims 2-7 and 9 are rejected on the ground of provisional obviousness-type double patenting as being unpatentable over claims 28-31, 33-37, 39, 52, 55, and 57-59 of copending Application No. 09/547,220. Applicants will consider filing a terminal disclaimer upon notice of allowable subject matter in this application.

## CONCLUSION

Entry of the foregoing amendments and remarks into the record of the above-identified application is respectfully requested. Applicants estimate that the remarks made herein place the pending claims in condition for allowance.

Respectfully submitted,

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